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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/147,693	02/17/1999	WERNER LUBITZ	P564-9005	2068

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EXAMINER

LEFFERS JR, GERALD G

ART UNIT PAPER NUMBER

1636

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/147,693

Applicant(s)

LUBITZ ET AL.

Examiner

Gerald G Leffers Jr., PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- ☒ Responsive to communication(s) filed on 05 April 2004.
- ☐ This action is FINAL. ☒ This action is non-final.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- ☒ Claim(s) 38-45, 49-62, 69, 70, 77 and 78 is/are pending in the application.
  - Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- ☒ Claim(s) 49 is/are allowed.
- ☒ Claim(s) 38-45, 50-62, 69, 70, 77 and 78 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- ☐ The specification is objected to by the Examiner.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
    - All
    - Some
    - None of:
      - ☐ Certified copies of the priority documents have been received.
      - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
      - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 4/5/2004.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/5/2004 has been entered.

In the response filed 4/5/2004 claims were amended (claims 39 and 49) and claims were cancelled (claims 63-65 & 71-72). Claims 38-45, 49-62, 69-70 and 77-78 are pending and under consideration in the instant application. Any rejection of record in the previous office actions not addressed herein is withdrawn. This action is not final.

### ***Information Disclosure Statement***

Receipt is acknowledged of an information disclosure statement (IDS) filed 4/5/2004. The signed and initialed PTO 1449 has been mailed along with this action.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 69-70, 77-78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the

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relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection. It is noted that this grounds of rejection would most likely be applicable to claims 50-62 if they were not dependent upon cancelled claim 46.**

The rejected claims are each drawn to a bacterial cell comprising a bacterial expression control sequence comprising an operator sequence from a lambdoid phage where the operator sequence has a different thermostability compared to a wild-type operator sequence with regard to binding of a repressor wherein the different thermostability results in repression of expression of a gene that is operatively linked to the operator sequence until a temperature is reached that is 3 to 10°C higher than the temperature at which the wildtype sequence is capable of repressing expression of the operatively linked gene. In short, each of the claims embraces a broad genus of operator sequences obtainable from literally any "lambdoid" phage that must meet the very specific functional limitation of binding a repressor (of any type) at temperatures 3 to 10°C higher than the temperature at which the wildtype operator sequence binds the same repressor.

The instant specification is enabling for screening for such mutant operator sequences, but only provides description of a single example of a mutated operator sequence that meets the functional limitations of the claims (i.e. SEQ ID NO: 2). No other sequence is given in the originally filed specification of any other mutated operator sequence that meets the functional limitations of the claims. Nor is any description provided of the domains within the broadly claimed class of lambdoid operator sequences that are well conserved among different lambda species and mutation of which would necessarily provide a mutant operator sequence that meets the functional limitations of the claims. Thus, the instant specification does not provide a

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structural/functional basis for the skilled artisan to envision the changes to a given lambdaoid operator sequence that will satisfy the functional limitations of the claims.

The approach taught by applicants for identifying mutated lambdaoid operator sequences that meet the functional limitations of the claims appears to be novel in the art. Therefore, the prior art does not offset the deficiencies of the instant specification with regard to providing a structural/functional basis for the skilled artisan to envision a sufficient number of specific operator sequences that meet the functional limitations of the rejected claims so as to describe the broadly claimed genus of such operator sequences.

Given that the rejected claims encompass a broad genus of operator sequences that must meet very specific functional limitations, and given that the instant specification and prior art do not provide a structural/functional basis for the skilled artisan to envision a sufficient number of specific embodiments of such operator sequences to describe the broadly claimed genus of operator sequences, the skilled artisan would not have been able to envision a sufficient number of mutated sequences that meet the thermostability requirements of the claims to describe the broadly claimed genus of such sequences. Therefore, the skilled artisan would have reasonably concluded applicants weren't in possession of the claimed invention at the time of filing.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 38-45, 50-62, 69-70 and 77-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new grounds of rejection.**

Each of the rejected claims recites the term “wild type” operator sequence. It is unclear what exactly is encompassed by this term. For example, does the term refer only to operator sequences that are found in “nature” or can it encompass other sequences? One of skill in the art, for example, would not normally consider the temperature-sensitive mutant cI857 as being a “wildtype” repressor. Yet, it appears from reading the instant application that the term “wildtype” operator sequence may be intended to mean any sequence that is mutated in the instant methods to produce an altered sequence with different thermostability characteristics. If this latter interpretation is correct, then it would be remedial to amend the claim language to somehow indicate that the first sequence is a starting sequence that is subsequently altered and that it is not necessarily some archetypical operator sequence found in “nature”.

Claim 38 is vague and indefinite in that the end result of the recited method does not recapitulate the preamble of the claim, making it unclear as to whether one has necessarily completed the method. The preamble states that the mutated operator sequence has a greater thermostability than the wildtype operator sequence with regard to binding to a repressor such that repression of a gene operatively linked to the mutated repressor until a temperature that is 3 to 10°C higher than the temperature at which the wildtype sequence is capable of repressing expression of an operatively linked gene. There is no positive action step, however, that necessarily relates back to this very specific functional limitation. It would be remedial to amend the claim to include a positive action step that directly relates back to this limitation (e.g. where mutated operator sequences are selected that mediate repression of expression of the operatively linked gene at a temperature that is 3 to 10°C higher than the temperature at which the wildtype sequence is capable of repressing expression of the operatively linked gene).

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Claim 38 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term “said DNA sequence” in line 4 of the claim. For example, OR, OL and wildtype operator sequences have been already recited in the claim. It would be remedial to amend the claim to clearly indicate that the term “said DNA sequence” refers to a mutated OR or OL sequence obtained from a lambdoid phage. Likewise, claims 69-70 are vague and indefinite in that there is no clear and positive prior antecedent basis for the term “said DNA sequence” in line 10 of claim 69 or in line 11 of claim 70, respectively.

Claim 50 is vague and indefinite in that it depends from a cancelled claim (i.e. claim 46).

Claims 69-70 are vague and indefinite in that the recitation of the generic term “compared to a wildtype sequence” are unclear. To what “wildtype” sequence is the comparison to be made?

Claims 77-78 are vague and indefinite in that it is unclear how these claims further limit the claims from which they depend. The claims recite the limitation of further comprising “a gene for a first cI repressor.” There is no clear and positive prior antecedent basis for the term “a” gene encoding a “first” cI repressor. Does the gene of claims 77-78 necessarily encode the “first” cI repressor that can bind the OR or OL operator sequence of part (a) of the claim, or can it be some other “first cI repressor”?

### ***Conclusion***

Claim 49 is allowed. No other claims are allowed.

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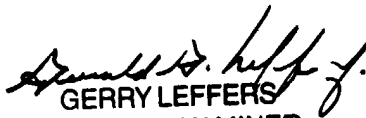
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD  
Primary Examiner  
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